AMENDMENT TO THE SPECIFICATION

Please enter the following amendments to the specification without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

Please delete the paragraph bridging pages 11-12 and replace it with the following paragraph:

Figure 2 shows the modifications of the HI loop of the fiber knob **(SEQ ID NO: 21)**. PCR-based mutagenesis was employed to delete a portion of the fiber gene encoding the hypervariable region of the HI loop **(SEQ ID NO: 22).** A unique *EcoRV* restriction site was incorporated in place of the deletion to allow the cloning of segments of DNA coding for heterologous protein sequences. In the fiber-FLAG protein, deleted amino acids of the HI loop were restored, and FLAG octapeptide was incorporated between threonine-546 and proline-547 **(SEQ ID NO: 23)**. The site of deletion is indicated by a filled triangle.

Please delete the paragraph bridging pages 26-27 and replace it with the following paragraph:

The present invention is directed towards a recombinant adenovirus, wherein the adenovirus comprises a fiber gene modified in the HI loop domain of the fiber knob. Preferably, the recombinant adenovirus can achieve CAR-independent gene transfer. Additionally, the adenovirus may further comprise an additional modification to the fiber knob, thereby ablating the native tropism of the adenovirus. Optimally, the modified fiber knob retains its ability to trimerize and retains its native biosynthesis profile. For instance, the fiber gene may be modified by introducing a ligand into the HI loop domain of the fiber knob, and representative examples of such ligands are physiological ligands, anti-receptor antibodies and cell-specific peptides. Preferred ligands the sequence Arg-Gly-Asp (RGD), more preferably, sequence CDCRGDCFC **(SEQ ID NO: 16)**. Furthermore, the adenoviral vector encoding the adenovirus further comprises a therapeutic gene, such as the herpes simplex virus-thymidine kinase gene.

Please delete the paragraph on page 28, lines 9-20, and replace it with the following paragraph:

The present invention is still further directed towards a method of increasing the ability of an adenovirus to transduce a cell, comprising the step of modifying the fiber gene in the HI loop domain of the fiber knob of the adenovirus. Preferably, the fiber gene is modified by introducing

a ligand into the HI loop domain of the fiber knob and representative ligands are physiological ligands, anti-receptor antibodies and cell-specific peptides. Preferably, the ligand has the sequence Arg-Gly-Asp (RGD), even more preferably the ligand has the sequence CDCRGDCFC **(SEQ ID NO: 16)**. Generally, the cell is a tumor cell, and may be *in vitro*, *in vivo* and *ex vivo*. Optimally, the adenoviral vector encoding the adenovirus further comprises a therapeutic gene.

Please delete the paragraph on page 50, line 19 to page 52, line 2 and replace it with the following paragraphs:

The transfer plasmids for the generation of recombinant baculoviruses expressing chimeric fibers were made as follows: a *BglII-MfeI* fragment from pQE.KNOB$_{HI}$FLAG was utilized to replace the *BglII-MfeI* fragment in the vector pBS.F5.UTR which has been described previously (25), thereby generating pBS.F5$_{HI}$FLAG. A *BssHII-XhoI* fragment from pBS.F5$_{HI}$FLAG was then cloned into the *BssHII-XhoI*-digested baculovirus transfer vector pFastBac1 (Life Technologies, Gaithersburg, Md.), resulting in pFB.F5$_{HI}$FLAG. To introduce the six-His **(SEQ ID NO: 18)** purification tag into the amino terminus of the chimeric fiber, the *BamHI-BssHII* fragment of pFB.F5$_{HI}$FLAG was replaced with a synthetic duplex made with oligonucleotides GATCCATGCATCACCATCACCATCACAAG (SEQ ID NO: 7) and CGCGCTTGTGATGGTGATGGTGATGCATG (SEQ ID NO: 8), which encodes MetHis$_6$Lys **(SEQ ID NO: 19)**. The resultant plasmid, pFB6H.F5$_{HI}$FLAG, contains the gene coding for a fiber with an amino-terminal six-His **(SEQ ID NO: 18)** tag and FLAG peptide inserted into the HI loop. To derive a similar plasmid containing the fiber gene with the HI loop coding sequence unmodified, the *BssHII-MfeI* fragment in pFB6H.F5$_{HI}$FLAG was replaced with homologous fragment from pNEB.PK3.6 (25), generating pFB6H.F5. In order to clone the gene encoding the fiber with the FLAG sequence in the HI loop into the fiber shuttle vector pNEB.PK3.6, a *BstXI-MfeI* fragment of the wild type fiber gene contained in this plasmid was replaced with a *BstXI-MfeI* fragment from pQE.KNOB$_{HI}$FLAG, thereby creating pNEB.F5$_{HI}$FLAG.

Please delete the paragraph bridging pages 54-55 and replace it with the following paragraph:

To derive a recombinant baculovirus expressing fiber-RGD, the transfer vector pFB.F5$_{HI}$FLAG was modified in a following way. First, *EcoRI* linker, CGG CGA ATT CGC **(SEQ ID NO: 20)**, was incorporated into *ClaI* site of pFB.F5$_{HI}$FLAG, resulting in pFB.F5.RI. Then, *NcoI-MunI*-fragment of pNEB.PK.F$_{HI}$RGD containing 3' portion of the fiber-RGD gene

was used to replace an *NcoI-MunI*-fragment in pFB.F5.RI, generating pFB.F5$_{HI}$RGD. This plasmid was then used to generate recombinant baculovirus genome via site-specific transposition by utilizing Bac-to-Bac kit (Gibco BRL, Gaithersburg, MD) according to manufacturer recommendations.